L1: Entry 27 of 96 File: USPT

DOCUMENT-IDENTIFIER: US 6159445 A
TITLE: Light imaging contrast agents

Brief Summary Text (16):
There are several patent publications which relate to light imaging technology and to the use of various dyes in light imaging: a labeling fluorescent dye comprising hydroxy aluminium 2,3-pyrido cyanide in JP 4,320,456 (Hitachi Chem), therapeutic and diagnostic agent for tumors containing fluorescent labelled phthalocyanine pigment in JP 4288 022 (Hitachi Chem), detection of cancer tissue using visible native luminescence in U.S. Pat. No. 4,930,516 (Alfano R. et al.), method and apparatus for detection of cancer tissue using native fluorescence in U.S. Pat. No. 5,131,398 (Alfano, R. et al.), improvements in diagnosis by means of fluorescenct light emmision from tissue in WO 90/10219 (Andersson-Engels, S. et al.), fluorescent porphyrin and fluorescent phthalocyanine-polyethylene glycol, polyol, and saccharide derivatives as fluorescent probes in WO91/18006 (Diatron Corp), method of imaging a random medium in U.S. Pat. No. 5,137,355 (State Univ. of New York), tetrapyrrole therapeutic agents in U.S. Pat. No. 5,066,274 (Nippon Petrochemicals), tetrapyrrole polyaminomonocarboxylic acid in therapeutic agents in U.S. Pat. No. 4,977,177 (Nippon Petrochemicals), tetrapyrrole aminocarboxylic acids in U.S. Pat. No. 5,004,811 (Nippon Petrochemicals), porphyrins and cancer treatment in U.S. Pat. No. 5,162,519 (Efamol Holdings), dihydroporphyrins and method of treating tumors susceptible to necrosis in U.S. Pat. No. 4,837,221 (Efamol), parenterally administered zinc phthalocyanide compounds in form of liposome dispersion containing synthetic phospholipids in EP 451 103 (CIBA Geigy), apparatus and method for detecting tumors in U.S. Pat. No. 4,515,165 (Energy Conversion Devices), time and frequency domain spectroscopy determining hypoxia in WO92/13598 (Nim Inc), phthalocyanatopolyethylene glycol and phthalocyanato saccharides as fluorescent digoxin reagent in WO 91/18007 (Diatron), fluorometer in U.S. Pat. No. 4,877,965 (Diatron), fiberoptic fluorescence spectrometer in WO 90/00035 (Yale Univ.), tissue oxygen measuring system in EP 502,270 (Hamamatsu Photonics), method for determining bilirubin concentration from skin reflectance in U.S. Pat. No. 4,029,084 (Purdue Research Foundation), bacteriochlorophyll-a derivative useful in photodynamic therapy in U.S. Pat. No. 5,173,504 (Health Research Inc), purified hematoporphyrin dimers and trimers useful in photodynamic therapy in U.S. Pat. No. 5,190,966 (Health Research Inc), drugs comprising porphyrins in U.S. Pat. No. 5,028,621 (Health Research Inc), hemoporphyrin derivatives and process of preparing in U.S. Pat. No. 4,866,168 (Health Research Inc), method to destroy or impair target cells in U.S. Pat. No. 5,145,863 (Health Research Inc), method to diagnose the presence or absence of tumor tissue in U.S. Pat. No. 5,015,463 (Health Research Inc), photodynamic therapeutic technique in U.S. Pat. No. 4,957,481 (U.S. Bioscience), apparatus for examining living tissue in U.S. Pat. No. 2,437,916 (Philip Morris and Company), transillumination method apparatus for the diagnosis of breast tumors and other breast lesions by normalization of an electronic image of the breast in U.S. Pat. No. 5,079,698 (Advanced Light Imaging Technologies), tricarbocyanine infrared absorbing dyes in U.S. Pat. No. 2,895,955 (Eastman Kodak), optical imaging system for neurosurgery in CA 2,048,697 (Univ. Techn. Int.), new porphyrin derivatives and their metallic complexes as photosensitizer for PDT in diagnosis and/or treatment of cancer in JP 323,597 (Hogyo,T), light receiving system of heterodyne detection and image forming device for light transmission image in EP 445,293 (Research Development Corp. of Japan), light receiving system of heterodyne detection and image forming device for light transmission image using light receiving system in WO 91/05239 (Research Development Corp. of Japan), storage-stable porphyrin compositions and a method for their

manufacture in U.S. Pat. No. 4,882,234 (Healux), method for optically measuring chemical analytes in WO 92/19957 (Univ. of Maryland at Baltimore), wavelength-specific cytotoxic agents in U.S. Pat. No. 4,883,790 (Univ. of British Columbia), hydro-monobenzo-porphyrin wavelength-specific cytotoxic agents in U.S. Pat. No. 4,920,143 (Univ. of British Columbia), apparatus and method for quantitative examination and high-resolution imaging of human tissue in EP 447,708 (Haidien Longxing Med Co), optical imaging system for neurosurgery in U.S. application Ser. No. 7,565,454 (University Technologies Int. Inc.), --characterization of specific drug receptors with fluorescent ligands in WO 93/03382 (Pharmaceutical Discovery Corp), 4,7-dichlorofluorescein dyes as molecular probes in U.S. Pat. No. 5,188,934 (Applied Biosystems), high resolution breast imaging device utilizing non-ionizing radiation of narrow spectral bandwith in U.S. Pat. No. 4,649,275 (Nelson, R. et al.), meso-tetraphenyl-porphyrin-Komplexverbindungen, Verfaren zu ihrer Herstellung und Diese Enthaltends Pharmazeutische Mittel in EP 336,879 (Schering), 13,17-propionsaure und propionsaurederivat Substituerte Porphyrin-Komplexverbindungen, Verfahren zu ihrer Herstellung und diese Enthaltende Pharmazeutische Mittel in EP 355,041 (Schering), photosensitizing agents in U.S. Pat. No. 5,093,349 (Health Research), pyropheophorbides and their use in photodynamic therapy in U.S. Pat. No. 5,198,460 (Health Research), optical histochemical analysis, in vivo detection and real-time guidance for ablation of abnormal tissues using Raman spectroscopic detection system in WO 93/03672 (Redd, D.), tetrabenztriazaporphyrin reagents and kits containing the same in U.S. Pat. No. 5,135,717 (British Technology Group), system and method for localization of functional activity in the human brain in U.S. Pat. No. 5,198,977 (Salb, J.). photodynamic activity of sapphyrins in U.S. Pat. No. 5,120,411 (Board of Regents, University of Texas), process for preparation of expanded porphyrins in U.S. Pat. No. 5,152,509 (Board of Regents, University of Texas), expanded porphyrins (Board of Regents, University of Texas), infrared radiation imaging system and method in WO 88/01485 (Singer Imaging), imaging using scattered and diffused radiation in WO 91/07655 (Singer Imaging), diagnostic apparatus for intrinsic fluorescence of malignant tumor in U.S. Pat. No. 4,957,114, indacene compounds and methods for using the same in U.S. Pat. No. 5,189,029 (Bo-Dekk Ventures), method of using 5,10,15,20-tetrakis (carboxy phenyl) porphine for detecting cancers of the lung in U.S. Pat. No. 5,162,231 (Cole, D. A. et al.), Verfahren zur Abbildung eines Gewebebereiches in DE 4327 798 (Siemens), chlorophyll and bacteriochlorophyll derivatives, their preparation and pharmaceutical compositions comprising them in EPO 584 552 (Yeda Research and Development Company), wavelength-specific photosensitive porphacyanine and expanded porphyrin-like compounds and methods for preparation and use thereof in WO 94/10172 (Qudra Logic Technologies), method and apparatus for improving the signal to noise ratio of an image formed of an object hidden in or behind a semiopaque random media in U.S. Pat. No. 5,140,463 (Yoo, K. M. et al.), benzoporphyrin derivatives for photodynamic therapy in U.S. Pat. No. 5,214,036 (University of British Columbia), fluorescence diagnostics of cancer using delta-amino levulinic acid in WO 93/13403 (Svanberg et al.), Verfahren zum Diagnostizieren von mit fluoreszierenden Substansen angereicherten, inbesondere tumorosen Gewebebereichen in DE 4136 769 (Humboldt Universitat), terpyridine derivatives in WO 90/00550 (Wallac).

Detailed Description Text (29):
Particulate materials in the form of liposomes have been suggested; liposome or LDL-administered Zn(II)-phthalocyanine has been suggested as photodynamic agent for tumors by Reddi, E. et al. in Lasers in Medical Science 5 (1990) 339, parenterally administered zinc phtalocyanine compositions in form of liposome dispersion containing synthetic phopholipid in EP 451 103 (CIBA Geigy) and liposome compositions containing benzoporphyrin derivatives used in photodynamic cancer therapy or an antiviral agents in CA 2,047,969 (Liposome Company). These particulate materials have been suggested as therapeutic agents and have nothing to do with scattering light imaging contrast agents.

Detailed Description Text (36):
Besides using liposomes as carriers for light imaging contrast agents, it is possible to use simple micelles, formed for example from surfactant molecules, such as sodium dodecyl sulphate, cetyltrimethylammonium halides, pluronics, tetronics etc., as carriers for photolabels which are moderately or substantially water insoluble but are solubilised by the amphiphilic micelle forming agent, e.g. photolabels such as indocyanine green. Similarly peptides such as PEG modified polyaspartic acid (see

Kwon et al. Pharm. Res. 10: 970 (1993)) which spontaneously aggregate into polymeric micelles may be used to carry such photolabels. Likewise photolabel carrier aggregate particles can be produced by treatment of polycyclic aromatic hydrocarbons with anionic surfactants (e.g. sodium dodecyl sulphate or sulphated pluronic F108) and subsequent addition of heavy metal ions (e.g. thorium or silver). Such heavy metal treatment gives rise to micelles exhibiting phosphorescent behaviour and these can be used in the present invention without incorporation of a photolabel, especially using a pulsed light source and gated detection of the temporally delayed phosphorescent light.

Detailed Description Text (40):
The particulate contrast agent used according to the invention may, as mentioned above, be non-photo-labelled or photolabelled. In the latter case this means that the particle either is an effective photoabsorber at the wavelength of the incident light (i.e. carries a chromophore) or is a fluorescent material absorbing light of the incident wavelength and emitting light at a different wavelength (i.e. carries a fluorophore). Examples of suitable fluorophores include fluorescein and fluorescein derivatives and analogues, indocyanine green, rhodamine, triphenylmethines, polymethines, cyanines, phalocyanines, naphthocyanines, merocyanines, lanthanide complexes (e.g. as in U.S. Pat. No. 4,859,777) or cryptates, etc. including in particular fluorophores having an emission maximum at a wavelength above 600 nm (e.g. fluorophores as described in WO-A-92/08722). Other labels include fullerenes, oxatellurazoles (e.g. as described in U.S. Pat. No. 4,599,410), LaJolla blue, porphyrins and porphyrin analogues (e.g. verdins, purpurins, rhodins, perphycenes, texaphyrins, sapphyrins, rubyrins, benzoporphyrins, photofrin, metalloporphyrins, etc.) and natural chromophores/fluorophores such as chlorophyll, carotenoids, flavonoids, bilins, phytochrome, phycobilins, phycoerythrin, phycocyanins, retinoic acid and analogues such as retinoins and retinates.

Detailed Description Text (74):
A solution of WIN 70177 (an iodinated contrast agent prepared according to Example 24 below) and, optionally fluoroscein in the molar ratio 100:1, optimally 50:1, most optimally 25:1, in DMSO (or DMF) is precipitated in water. The resulting precipitate is milled as described in U.S. Pat. No. 5,145,684 together with a surfactant stabilizer (eg. Pluronic F108 or Tetronic T-908 or 1508) to a particle size of 0.2 .mu.m and dispersed in an aqueous medium to a contrast agent concentration of 0.5 to 25% by weight and a surfactant content of 0.1 to 30% by weight. A cloud point modifier such as polyethylene glycol 400 (PEG 400) or propylene glycol as disclosed in U.S. Pat. No. 5,352,459 may also be included to ensure stability on autoclave stabilization.

Detailed Description Text (77):
Phytochrome is added to an aqueous solution of sodium dodecyl sulphate (pH>10). The resulting solution is added to a stirred solution of acetic acid containing a surfactant (selected from PVP, pluronics and tetronics) and the mixture is diafiltered to remove soluble salts, excess acid etc. from the suspension yielding a dispersion of 10-100 nm particles.

Detailed Description Text (80):
Indocyanine green (ICG) (0.1 to 10%) is mixed with 3% Pluronic F108 in aqueous solution to form a micellar composition which is sterile filtered.

Detailed Description Text (90):
WIN 70146 (an iodinated X-ray contrast agent prepared according to Example 23 below) was added to each of 3.times.1.5 oz brown glass bottles containing approximately 12 ml of zirconium silicate, 1.1 mm diameter beads in an amount sufficient to be 15% (wt/vol %) of the final suspension. Bottle A was also made 3% (wt/vol %) Pluronic F-68 while bottle B was made 3% (wt/vol %)) Pluronic F-108 and bottle C was made 3% (wt/vol %) Tetronic T-908. The resulting suspensions were milled at approx 150 rpm for a total of 9 days with estimates of particle size determined at various intervals as detailed below.

Detailed Description Text (93):
Preparation and Acute Safety Testing of Nanoparticle Suspensions of WIN 70146 in Pluronic F108

Detailed Description Text (97):
Preparation of WIN 70146 in Pluronic F108 (I-404)

Detailed Description Text (98):
WIN 70146 was milled with 1.1 mm diameter zirconium silicate beads for 3 days under aseptic conditions. The concentration of this agent was 15% WIN 70146 in the presence of 4% Pluronic F-108. No additional salts or surfactants were added. The average particle size of the resulting nanoparticle suspension was 162 nm as determined by light scattering.

Detailed Description Text (100):
Preparation of an Autoclavable Formulation of WIN 70146 Using Pluronic F-108 and PEG 400

Detailed Description Text (101):
WIN 70146 was milled with 1.1 mm diameter zirconium silicate beads in the presence of Pluronic F-108 for 3 days. The final particle size was determined to be 235 nm. At this point, sterile PEG 400 was added to the suspension such that at completion, the formulation contained 15% (wt/vol %) WIN 70146, 3% (wt/vol %) Pluronic F-108 and 10% PEG 400. This formulation was then autoclaved under standard conditions (ie. 121 degrees C. for 20 min.) resulting in a final particle size of 248 nm.

Detailed Description Text (108):
A formulation of WIN 70177 (an iodinated X-ray contrast agent prepared according to Example 24) was prepared as 15 gm of WIN 70177/100 ml of suspension and 4.25 gm of Pluronic F108/100 ml of suspension and 10 gm of PEG 400/100 ml of suspension. The suspension was milled for 5 days after which the average particle size was determined by light scattering to be about 235 nm. Stability testing in fresh rat plasma and simulated gastric fluid did not show any aggregation.

Detailed Description Text (115):
A formulation of WIN 67722 (an iodinated X-ray contrast agent as described in U.S. Pat. No. 5,322,679) was prepared as in Example 1 using 3% Pluronic F108 and 15% PEG 1450. The suspension was milled for 3 days and achieved a particle size of 213 nm (small fraction at 537 nm) as determined by light scattering with a Coulter N4MD particle sizer.

Detailed Description Text (118):
A nanoparticle suspension of WIN 67722 was prepared as in Example 17 using 3% Pluronic F108 and 15% PEG 1450 which after autoclaving gave particles with an average diameter of 214 nm. This suspension was then diluted in water to various levels listed below. The per cent of incident light transmitted was then determined for each suspension at several wavelengths (see below). The suspensions were then dissolved by addition of methanol and examined for per cent transmitted light against an equivalent solvent blank. The results are given below.

Detailed Description Text (122):
Nanoparticle WIN 72115 (a fluorescent iodinated contrast agent as described in Example 21 below) was prepared by combining WIN 72115 and Pluronic F108 (BASF, Parsippany, N.J.) in a glass jar at concentrations of 15 gm/100 ml suspension and 3 gm/100 ml suspension. The jar was then half filled with 1.0 mm diameter zirconium silicate beads and sufficient water added to complete the required concentrations of agent/surfactant as noted above. Alternatively, the surfactant can be dissolved in the water before addition to the jar (with or without sterile filtration through 0.2 micron filters).

L2: Entry 3 of 4 File: USPT

DOCUMENT-IDENTIFIER: US 5270053 A
TITLE: Parenterally administerable liposome formulation comprising synthetic lipid

Brief Summary Text (9):
The preparation of liposome dispersions by other methods that do not use organic solvents also gives rise to problems. Even when solvent-free dry preparations, such as lyophilisates or evaporation residues, are used for the formation of the aqueous liposome dispersions, the preparation of those dry preparations can in turn be effected only from solutions in selected organic solvents or solvent mixtures because of the lipophilic nature and the water-insolubility of the lipid components. Both the zinc-phthalocyanine complex and the phospholipids used have to be completely soluble in those solvents. The evaporation of the solvents must result in a homogeneous and pourable powder. The components must not be allowed to separate, as this would result in the agglutination of the dry preparation and the formation not of liposomes but only of poorly dispersible aggregates, for example large micelles, which could cause embolisms.

Brief Summary Text (40):
In the pharmaceutically acceptable carrier liquid d) the components a) and b) or a), b) and c) are present in the form of liposomes, preferably multilamellar liposomes, in such a manner that for several days or weeks there is no re-formation of solids or solid aggregates, such as micelles, and the clear or in some cases slightly opalescent liquid comprising the said components can be administered, if necessary after filtration, parenterally, preferably intravenously.

Brief Summary Text (42):
Suitable water-soluble excipients in the solution and in the dry preparation are also wetting agents or surfactants in the true sense that can be used for liquid pharmaceutical formulations, especially non-ionic surfactants of the fatty acid polyhydroxy alcohol ester type, such as sorbitan monolaurate, monooleate, monostearate or monopalmitate, sorbitan tristearate or trioleate, polyoxyethylene adducts of fatty acid polyhydroxy alcohol esters, such as polyoxyethylene sorbitan monolaurate, monooleate, monostearate, monopalmitate, tristearate or trioleate, polyethylene glycol fatty acid esters, such as polyoxyethyl stearate, polyethylene glycol 400 stearate, polyethylene glycol 2000 stearate, especially ethylene oxide/propylene oxide block polymers of the Pluronic.RTM. type (Wyandotte Chem. Corp.) or Synperonic.RTM. type (ICI).

Other Reference Publication (8):
CA 112:240366y, Ginerva, et al, "Delivery of the tumor photosensitizer zinc(II)phthalocyanine . . . " (1990).

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☐ 1. Document ID: US 6159445 A

L2: Entry 1 of 4 File: USPT

US-PAT-NO: 6159445
DOCUMENT-IDENTIFIER: US 6159445 A

TITLE: Light imaging contrast agents

DATE-ISSUED: December 12, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Klaveness; Jo	Oslo			NO
Fuglass; Bjorn	Oslo			NO
Rongved; P.ang.al	Oslo			NO
Johannesen; Edvin	Oslo			NO
Henrichs; Paul Mark	Wayne	PA		
Heinrich; Wolfgang Hans	Wayne	PA		
Bacon; Edward Richard	Wayne	PA		
Toner; John Luke	Wayne	PA		
McIntire; Gregory Lynn	Wayne	PA		
Desai; Vinay C.	Pheonixville	PA		

US-CL-CURRENT: 424/9.6; 424/9.1, 600/314, 600/317, 600/473, 600/476

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

☐ 2. Document ID: US 6123923 A

L2: Entry 2 of 4 File: USPT

US-PAT-NO: 6123923
DOCUMENT-IDENTIFIER: US 6123923 A

TITLE: Optoacoustic contrast agents and methods for their use

DATE-ISSUED: September 26, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Unger; Evan C.	Tucson	AZ		
Wu; Yunqiu	Tucson	AZ		

US-CL-CURRENT: 424/9.52; 424/450, 424/9.1, 424/9.2, 424/9.3, 424/9.6, 514/410

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
Draw Desc | Image

☐ 3. Document ID: US 5270053 A

L2: Entry 3 of 4 File: USPT

US-PAT-NO: 5270053
DOCUMENT-IDENTIFIER: US 5270053 A

TITLE: Parenterally administerable liposome formulation comprising synthetic lipid

DATE-ISSUED: December 14, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Schneider; Peter	Bottmingen			CH
van Hoogevest; Peter	Riehen			CH
Capraro; Hans G.	Rheinfelden			CH
Isele; Ute	Bad Bellingen			DE

US-CL-CURRENT: 424/450; 424/641, 428/402.2, 514/185

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC
Draw Desc | Image

☐ 4. Document ID: US 4511641 A

L2: Entry 4 of 4 File: USPT

US-PAT-NO: 4511641
DOCUMENT-IDENTIFIER: US 4511641 A

TITLE: Metal film imaging structure

DATE-ISSUED: April 16, 1985

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Busman; Stanley C.	Oakdale	MN		
Chang; John C.	New Brighton	MN		

US-CL-CURRENT: 430/158; 430/142, 430/143, 430/161, 430/162, 430/166, 430/252, 430/253, 430/254, 430/257, 430/258, 430/259, 430/271.1, 430/273.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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L3: Entry 4 of 4 File: USPT

DOCUMENT-IDENTIFIER: US 4125503 A
TITLE: Ultraviolet curing emulsion systems

Detailed Description Text (2):
50 parts of an epoxy diacrylate made by reacting hydroxy ethyl acrylate with a diglycidyl ether of bisphenol A having a molecular weight of about 390 is dissolved in 50 parts of butyl carbamoyl ethyl acrylate, and the solution is mixed with 5 parts of benzophenone photosensitizer and 10 parts of Pluronic F 127 emulsifier. This mixture is subjected to high speed agitation and 100 parts of deionized water is added slowly to produce an emulsion having an average particle size of less than about 1 micron.

L4: Entry 5 of 26 File: USPT

DOCUMENT-IDENTIFIER: US 6123923 A
TITLE: Optoacoustic contrast agents and methods for their use

Detailed Description Text (28):
"Photoactive agent" refers to any compound or material that is active in light or that responds to light, including, for example, chromophores (e.g., materials that absorb light at a given wavelength), fluorophores (e.g., materials that emit light at a given wavelength), photosensitizers (e.g., materials that can cause necrosis of tissue and/or cell death in vitro and/or in vivo), fluorescent materials, phosphorescent materials and the like, that may be used in diagnostic or therapeutic applications. "Light" refers to all sources of light including the ultraviolet (UV) region, the visible region and/or the infrared (IR) region of the spectrum.

Detailed Description Text (50):
The term "photoactive agent" includes fluorescent materials, phosphorescent materials, photosensitizers, chromophores, fluorophores and the like. Photoactive agents that are useful in optoacoustic contrast agents can be chosen from materials having relatively high molar absorptivities, such as greater than about 10.sup.5 c.sup.-1 M.sup.-1, with absorption maxima preferably from about 500 nm to about 1400 nm, more preferably from about 730 nm to about 1300 nm. For photoactive materials used in imaging regions of a patient and/or diagnosing the presence of diseased tissue in a patient, fluorescence quantum yield is a critical consideration and is preferably maximized. Preferred photoactive agents are highly fluorometrically active and yield a high quantum percentage of light when energized at the appropriate wavelength. The photoactive agents may be active in the UV region, the visible region and/or the IR region of the spectrum, preferably in the IR region. For imaging regions of a patient and/or diagnosing the presence of diseased tissue in a patient, the photoactive material is preferably a fluorescent material.

Detailed Description Text (52):
Preferably, the photoactive agent that is used for therapeutic applications is a photosensitizer. Photosensitizers have shown great promise in cancer therapy. See, for example, Peng et al, Ultrastructural Pathology, 20:109 (1996), Reddi, J. Photochem. Photobiol. B: Biol., 37:189 (1997), Jori, J. Photochem. Photobiol. B: Biol., 36:87 (1996), Calzavara-Pinton et al, J. Photochem. Photobiol. B: Biol., 36:225 (1996), Geze et al, J. Photochem. Photobiol. B: Biol., 20:23 (1993) and Spikes, J. Photochem. Photobiol. B: Biol., 6:259 (1990), the disclosures of each of which are hereby incorporated by reference herein in their entirety. Upon application of the appropriate light, photosensitizers can photochemically (e.g., through photooxidation, photoreduction and the like) change into a form that is toxic to the surrounding tissue. For example, following excitation of a photosensitizer to a long-lived excited singlet and/or triplet state, a targeted tumor is destroyed either by the highly reactive singlet oxygen species (a Type II mechanism) and/or by free radical products (a Type I mechanism) generated by quantum energy transfer. Major biological target molecules of the singlet oxygen species and/or free radical products include nucleic acids, enzymes and cell membranes. A secondary therapeutic effect of the present methods involves the release of pathophysiologic products such as prostaglandins, thromboxanes and leukotrienes by tissue exposed to the effects of activated photosensitizers. Thus, it will be apparent to one skilled in the art that careful targeting of the photoactive agents is of paramount importance to achieve therapeutic effects without toxemias.

Detailed Description Text (53):
Irradiation of the photoactive agents, including fluorescent materials and therapeutic photosensitizers, may be applied interstitially, superficially, intravascularly and/or with the aid of light conductors, such as fiber optics. The wavelength and intensity of irradiation to be applied will depend upon the particular photoactive agents being used, since different photoactive agents have different optimal wavelengths of response. Thus, the requisite wavelength and intensity of irradiation may be readily determined by one skilled in the art based upon the particular photoactive agents being used.

Detailed Description Text (54):
Suitable photoactive agents that may be used in the present invention include, for example, fluoresceins, indocyanine green, rhodamine, triphenylmethines, polymethines, cyanines, fullerenes, oxatellurazoles, verdins, rhodins, perphycenes, sapphyrins, rubyrins, cholesteryl 4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene-3-dodecanoate, cholesteryl 12-(N-methyl-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-dodecanate, cholesteryl cis-parinarate, cholesteryl 3-((6-phenyl)-1,3,5-hexatrienyl)phenyl-proprionate, cholesteryl 1-pyrenebutyrate, cholesteryl 1-pyrenedecanoate, cholesteryl 1-pyrenehexanoate, 22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-ol, 22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-yl cis-9-octadecenoate, 1-pyrenemethyl 3-(hydroxy-22,23-bisnor-5-cholenate, 1-pyrene-methyl 3.beta.-(cis-9-octadecenoyloxy)-22,23-bisnor-5-cholenate, acridine orange 10-dodecyl bromide, acridine orange 10-nonyl bromide, 4-(N,N-dimethyl-N-tetradecylammonium)-methyl-7-hydroxycoumarin) chloride, 5-dodecanoylaminofluorescein, 5-dodecanoyl-aminofluorescein-bis-4,5-dimethoxy-2-nitrobenzyl ether, * 2-dodecylresorufin, fluorescein octadecyl ester, 4-heptadecyl-7-hydroxycoumarin, 5-hexadecanoylaminoeosin, 5-hexadecanoylaminofluorescein, 5-octadecanoylaminofluorescein, N-octadecyl-N'-(5-(fluoresceinyl))thiourea, octadecyl rhodamine B chloride, 2-(3-(diphenylhexatrienyl)-propanoyl)-1-hexadecanoyl-sn-glycero- 3-phosphocholine, 6-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)hexanoic acid, 1-hexadecanoyl-2-(1-pyrenedecanoyl)-sn-glycero-3-phosphocholine, 1,1'-dioctadecyl-3,3,3',3'-tetramethyl-indocarbocyanine perchlorate, 12-(9-anthroyloxy)oleic acid, 5-butyl-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene-3-nonanoic acid, N-(lissamine.TM. rhodamine B sulfonyl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt, phenylglyoxal monohydrate, naphthalene-2,3-dicarboxaldehyde, 8-bromomethyl-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indace ne, o-phthaldialdehyde, lissamine.TM. rhodamine B sulfonyl chloride, 2',7'-difluorofluorescein, 9-anthronitrile, 1-pyrenesulfonyl chloride, 4-(4-(dihexadecylamino)-styryl)-N-methylpyridinium iodide, chlorins, such as chlorin, chlorin e6, bonellin, mono-L-aspartyl chlorin e6, mesochlorin, meso-tetraphenylisobacteriochlorin, and meso-tetraphenylbacteriochlorin, hypocrellin B, purpurins, such as octaethylpurpurin, zinc(II) etiopurpurin, tin(IV) etiopurpurin and tin ethyl etiopurpurin, lutetium texaphyrin, photofrin, metalloporphyrins, protoporphyrin IX, tin protoporphyrin, benzoporphyrin, haematoporphyrin, phthalocyanines, naphthocyanines, merocyanines, lanthanide complexes, silicon phthalocyanine, zinc phthalocyanine, aluminum phthalocyanine, Ge octabutyoxyphthalocyanines, methyl pheophorbide-.alpha.-(hexyl-ether), porphycenes, ketochlorins, sulfonated tetraphenylporphines, .delta.-aminolevulinic acid, texaphyrins, including, for example, 1,2-dinitro-4-hydroxy-5-methoxybenzene, 1,2-dinitro-4-(1-hydroxyhexyl)oxy-5-methoxybenzene, 4-(1-hydroxyhexyl)oxy-5methoxy-1,2-phenylenediamine, and texaphyrin-metal chelates, including the metals Y(III), Mn(II), Mn(III), Fe(II), Fe(III) and the lanthanide metals Gd(III), Dy(III), Eu(III), La(III), Lu(III) and Tb(III), chlorophyll, carotenoids, flavonoids, bilins, phytochromes, phycobilins, phycoerythrins, phycocyanines, retinoic acids, retinoins, retinates, or combinations of any of the above. One skilled in the art will readily recognize or can readily determine which of the above compounds are, for example, fluorescent materials and/or photosensitizers. Lissamine.TM. is the trademark for N-ethyl-N-[4-[[4-[ethyl [(3-sulfophenyl)methyl]-amino]phenyl](4-sulfophenyl)-methylene]-2,5-cycloh exadien-1-ylidene]-3-sulfobenzene-methanaminium hydroxide, inner salt, disodium salt

and/or ethyl[4-[p[ethyl(m-sulfobenzyl)amino]-.alpha.-(p-sulfophenyl)benzylidene]-2,5-cyclohexadien-1-ylidene](m-sulfobenzyl)ammonium hydroxide inner salt disodium salt (commercially available from Molecular Probes, Inc., Eugene, Oreg.).

Detailed Description Text (57):
Antibody-bound photoactive agents or photosensitizers may be used where an immune response to the presence of the antibody is desired, including those described, for example, by Ebato et al, Anal. Chem., 66:1683-1689 (1994), the disclosure of which is hereby incorporated by reference herein in its entirety.

Detailed Description Text (76):
A wide variety of lipids may be used as stabilizing materials and vesicles in the present invention. The lipids may be of either natural, synthetic or semi-synthetic origin, including for example, fatty acids, fluorinated lipids, neutral fats, phosphatides, oils, fluorinated oils, glycolipids, surface active agents (surfactants and fluorosurfactants), aliphatic alcohols, waxes, terpenes and steroids. Suitable lipids which may be used to prepare the stabilizing materials of the present invention include, for example, fatty acids, lysolipids, fluorinated lipids, phosphocholines, such as those associated with platelet activation factors (PAF) (Avanti Polar Lipids, Alabaster, Ala.), including 1-alkyl-2-acetoyl-sn-glycero 3-phosphocholines, and 1-alkyl-2-hydroxy-sn-glycero 3-phosphocholines, which target blood clots; phosphatidylcholine with both saturated and unsaturated lipids, including dioleoylphosphatidylcholine; dimyristoylphosphatidylcholine; dipentadecanoylphosphatidylcholine; dilauroylphosphatidylcholine; dipalmitoylphosphatidylcholine (DPPC); distearoylphosphatidylcholine (DSPC); and diarachidonylphosphatidylcholine (DAPC); phosphatidylethanolamines, such as dioleoylphosphatidylethanolamine, dipalmitoylphosphatidylethanolamine (DPPE) and distearoylphosphatidylethanolamine (DSPE); phosphatidylserine; phosphatidylglycerols, including distearoylphosphatidyl-glycerol (DSPG); phosphatidylinositol; sphingolipids such as sphingomyelin; glycolipids such as ganglioside GM1 and GM2; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids, such as dipalmitoylphosphatidic acid (DPPA) and distearoyl-phosphatidic acid (DSPA); palmitic acid; stearic acid; arachidonic acid; oleic acid; lipids bearing polymers, such as chitin, hyaluronic acid, polyvinylpyrrolidone or polyethylene glycol (PEG), also referred to as "pegylated lipids" with preferred lipid bearing polymers including DPPE-PEG (DPPE-PEG), which refers to the lipid DPPE having a PEG polymer attached thereto, including, for example, DPPE-PEG5000, which refers to DPPE having attached thereto a PEG polymer having a mean average molecular weight of about 5000; lipids bearing sulfonated mono-, di-, oligo- or polysaccharides; cholesterol, cholesterol sulfate and cholesterol hemisuccinate; tocopherol hemisuccinate; lipids with ether and ester-linked fatty acids; polymerized lipids (a wide variety of which are well known in the art); diacetyl phosphate; dicetyl phosphate; stearylamine; cardiolipin; phospholipids with short chain fatty acids of about 6 to about 8 carbons in length; synthetic phospholipids with asymmetric acyl chains, such as, for example, one acyl chain of about 6 carbons and another acyl chain of about 12 carbons; ceramides; non-ionic liposomes including niosomes such as polyoxyalkylene (e.g., polyoxyethylene) fatty acid esters, polyoxy-alkylene (e.g., polyoxyethylene) fatty alcohols, polyoxyalkylene (e.g., polyoxyethylene) fatty alcohol ethers, polyoxyalkylene (e.g., polyoxyethylene) sorbitan fatty acid esters (such as, for example, the class of compounds referred to as TWEEN.RTM., including, for example, TWEEN.RTM. 20, TWEEN.RTM.40 and TWEEN.RTM. 80, commercially available from ICI Americas, Inc., Wilmington, Del.), glycerol polyethylene glycol oxystearate, glycerol polyethylene glycol ricinoleate, alkyloxylated (e.g., ethoxylated) soybean sterols, alkyloxylated (e.g., ethoxylated) castor oil, polyoxyethylene-polyoxypropylene polymers, and polyoxyalkylene (e.g., polyoxyethylene) fatty acid stearates; sterol aliphatic acid esters including cholesterol sulfate, cholesterol butyrate, cholesterol isobutyrate, cholesterol palmitate, cholesterol stearate, lanosterol acetate, ergosterol palmitate, and phytosterol n-butyrate; sterol esters of sugar acids including cholesterol glucuronide, lanosterol glucuronide, 7-dehydrocholesterol glucuronide, ergosterol glucuronide, cholesterol gluconate, lanosterol gluconate, and ergosterol gluconate; esters of sugar acids and alcohols including lauryl glucuronide, stearoyl glucuronide, myristoyl glucuronide, lauryl gluconate, myristoyl gluconate, and stearoyl gluconate; esters of sugars and aliphatic acids including sucrose laurate, fructose laurate, sucrose palmitate, sucrose stearate, glucuronic acid, gluconic acid and polyuronic acid; saponins including sarsasapogenin,

smilagenin, hederagenin, oleanolic acid, and digitoxigenin; glycerol dilaurate, glycerol trilaurate, glycerol dipalmitate, glycerol and glycerol esters including glycerol tripalmitate, glycerol distearate,

Detailed Description Text (94):
In addition to stabilizing materials and/or vesicles formulated from lipids and/or proteins, embodiments of the present invention may also involve stabilizing materials or vesicles formulated from polymers which may be of natural, semi-synthetic (modified natural) or synthetic origin. Polymer denotes a compound comprised of two or more repeating monomeric units, and preferably 10 or more repeating monomeric units. Semi-synthetic polymer (or modified natural polymer) denotes a natural polymer that has been chemically modified in some fashion. Suitable natural polymers include naturally occurring polysaccharides, such as, for example, arabinans, fructans, fucans, galactans, galacturonans, glucans, mannans, xylans (such as, for example, insulin), levan, fucoidan, carrageenan, galatocarolose, pectic acid, pectins, including amylose, pullulan, glycogen, amylopectin, cellulose, dextran, dextrin, dextrose, glucose, polyglucose, polydextrose, pustulan, chitin, agarose, keratin, chondroitin, dermatan, hyaluronic acid, alginic acid, xanthin gum, starch and various other natural homopolymer or heteropolymers, such as those containing one or more of the following aldoses, ketoses, acids or amines: erythrose, threose, ribose, arabinose, xylose, lyxose, allose, altrose, glucose, dextrose, mannose, gulose, idose, galactose, talose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, mannitol, sorbitol, lactose, sucrose, trehalose, maltose, cellobiose, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, glucuronic acid, gluconic acid, glucaric acid, galacturonic acid, mannuronic acid, glucosamine, galactosamine, and neuraminic acid, and naturally occurring derivatives thereof. Accordingly, suitable polymers include, for example, proteins, such as albumin. Exemplary semi-synthetic polymers include carboxymethyl-cellulose, hydroxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, and methoxycellulose. Exemplary synthetic polymers include polyphosphazenes, polyalkylenes (e.g., polyethylene), such as, for example, polyethylene glycol (including, for example, the class of compounds referred to as PLURONICS.RTM., commercially available from BASF, Parsippany, N.J.), polyoxyalkylenes (e.g., polyoxyethylene), and polyethylene terephthlate, polypropylenes (such as, for example, polypropylene glycol), polyurethanes (such as, for example, polyvinyl alcohol (PVA), polyvinyl chloride and polyvinyl-pyrrolidone), polyamides including nylon, polystyrene, polylactic acids, fluorinated hydrocarbon polymers, fluorinated carbon polymers (such as, for example, polytetrafluoroethylene), acrylate, methacrylate, and polymethylmeth-acrylate, and derivatives thereof. Preferred are synthetic polymers or copolymers prepared from monomers, such as acrylic acid, methacrylic acid, ethyleneimine, crotonic acid, acrylamide, ethyl acrylate, methyl methacrylate, 2-hydroxyethyl methacrylate (HEMA), lactic acid, glycolic acid, c-caprolactone, acrolein, cyanoacrylate, bisphenol A, epichlorhydrin, hydroxyalkylacrylates, siloxane, dimethylsiloxane, ethylene oxide, ethylene glycol, hydroxyalkyl-methacrylates, N-substituted acrylamides, N-substituted methacrylamides, N-vinyl-2-pyrrolidone, 2,4-pentadiene-1-ol, vinyl acetate, acrylonitrile, styrene, p-amino-styrene, p-amino-benzyl-styrene, sodium styrene sulfonate, sodium 2-sulfoxyethylmethacrylate, vinyl pyridine, aminoethyl methacrylates, 2-methacryloyloxytri-methylammonium chloride, and polyvinylidene, as well polyfunctional crosslinking monomers such as N,N'-methylenebis-acrylamide, ethylene glycol dimethacrylates, 2,2'-(p-phenylenedioxy)diethyl dimeth-acrylate, divinylbenzene, triallylamine and methylenebis(4-phenylisocyanate), including combinations thereof. Preferable polymers include polyacrylic acid, polyethyleneimine, polymethacrylic acid, polymethylmethacrylate, polysiloxane, polydimethylsiloxane, polylactic acid, poly(.epsilon.-caprolactone), epoxy resin, poly(ethylene oxide), poly(ethylene glycol), and polyamide (nylon) polymers. Preferable copolymers include polyvinylidene-polyacrylonitrile, polyvinylidene-polyacrylonitrile-polymethyl-methacrylate, polystyrene-polyacrylonitrile and poly d-1, lactide co-glycolide polymers; most preferably polyvinylidene-polyacrylonitrile. Other suitable monomers and polymers will be apparent to one skilled in the art in view of the

Detailed Description Text (110):
where x is an integer of from about 6 to about 12; preferably from about 8 to about 10; more preferably 9; z is an integer of from about 8 to about 20; preferably from

about 8 to about 16; more preferably from about 8 to about 12; still more preferably from about 8 to about 10; most preferably about 9; and A is a monosaccharide or a disaccharide. Suitable monosaccharides and disaccharides include, for example, allose, altrose, glucose, dextrose, mannose, glycerose, gulose, idose, galactose, talose, fructose, psicose, sorbose, rhamnose, tagatose, ribose, arabinose, xylose, lyxose, ribulose, xylulose, erythrose, threose, erythrulose, fucose, sucrose, lactose, maltose, isomaltose, trehalose, cellobiose and the like. Preferably, the monosaccharide or disaccharide is glucose, dextrose, fructose, mannose, galactose, glucosamine, galactosamine, maltose, sucrose or lactose.

Detailed Description Text (127):
In addition to residues of hydrophilic polymers, Z in formula (IV) can be a saccharide residue. Exemplary saccharides from which Z can be derived include, for example, monosaccharides or sugar alcohols, such as erythrose, threose, ribose, arabinose, xylose, lyxose, fructose, sorbitol, mannitol and sedoheptulose, with preferred monosaccharides being fructose, mannose, xylose, arabinose, mannitol and sorbitol; and disaccharides, such as lactose, sucrose, maltose and cellobiose. Other saccharides include, for example, inositol and ganglioside head groups. Other suitable saccharides, in addition to those exemplified above, will be readily apparent to one skilled in the art based on the present disclosure. Generally, saccharides from which Z is derived include saccharides that can be incorporated in the fluorinated amphiphilic compounds via alkylation or acylation reactions.

Detailed Description Text (149):
The stabilizing materials and/or vesicles used in the present invention may be controlled according to size, solubility and heat stability by choosing from among the various additional or auxiliary stabilizing materials described herein. These materials can affect the parameters of the vesicles, especially vesicles formulated from lipids, not only by their physical interaction with the membranes, but also by their ability to modify the viscosity and surface tension of the surface of the vesicle. Accordingly, the vesicles used in the present invention may be favorably modified and further stabilized, for example, by the addition of one or more of a wide variety of (i) viscosity modifiers, including, for example, carbohydrates and their phosphorylated and sulfonated derivatives; polyethers, preferably with molecular weight ranges between 400 and 100,000; and di- and trihydroxy alkanes and their polymers, preferably with molecular weight ranges between 200 and 50,000; (ii) emulsifying and/or solubilizing agents including, for example, acacia, cholesterol, diethanolamine, glyceryl monostearate, lanolin alcohols, lecithin, mono- and di-glycerides, mono-ethanolamine, oleic acid, oleyl alcohol, poloxamer, for example, poloxamer 188, poloxamer 184, poloxamer 181, PLURONICS.RTM. (BASF, Parsippany, N.J.), polyoxyethylene 50 stearate, polyoxyl 35 castor oil, polyoxyl 10 oleyl ether, polyoxyl 20 cetostearyl ether, polyoxyl 40 stearate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, propylene glycol diacetate, propylene glycol monostearate, sodium lauryl sulfate, sodium stearate, sorbitan mono-laurate, sorbitan mono-oleate, sorbitan mono-palmitate, sorbitan monostearate, stearic acid, trolamine, and emulsifying wax; (iii) suspending and/or viscosity-increasing agents, including, for example, acacia, agar, alginic acid, aluminum mono-stearate, bentonite, magma, carbomer 934P, carboxymethyl-cellulose, calcium and sodium and sodium 12, carrageenan, cellulose, dextran, gelatin, guar gum, locust bean gum, veegum, hydroxyethyl cellulose, hydroxypropyl methyl-cellulose, magnesium-aluminum-silicate, ZEOLITES.RTM., methylcellulose, pectin, polyethylene oxide, povidone, propylene glycol alginate, silicon dioxide, sodium alginate, tragacanth, xanthan gum, .alpha.-d-gluconolactone, glycerol and mannitol; (iv) synthetic suspending agents, such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), polyvinylalcohol (PVA), polypropylene glycol (PPG), and polysorbate; and (v) tonicity raising agents which stabilize and add tonicity, including, for example, sorbitol, mannitol, trehalose, sucrose, propylene glycol and glycerol.

Detailed Description Text (243):
In the case of targeting ligands which comprise saccharide groups, suitable saccharide moieties include, for example, monosaccharides, disaccharides and polysaccharides. Exemplary monosaccharides may have six carbon atoms and these saccharides include allose, altrose, glucose, dextrose, mannose, gulose, idose, galactose, talose, fructose, psicose, verbose and tagatose. Five carbon saccharides include ribose, arabinose, xylose, lyxose, ribulose and xylulose. Four carbon

saccharides include erythrose, threose and erythrulose. Disaccharides include sucrose, lactose, maltose, isomaltose and cellobiose. Saccharide bearing targeting lipids may be synthesized through a multistep organic synthesis approach, as described more fully hereinafter. For example, lipids bearing targeting glucose moieties may be prepared by reacting, for example, .alpha.-glucopyranosyl bromide tetrabenzyl with .omega.-trifluoroacetyl-aminopoly-ethyleneglycol to obtain .omega.-glucopyranosyl tetrabenzyl-.omega.'-trifluoroacetyl-aminopolyethyleneglycol. This may then be hydrolyzed in a sodium carbonate or potassium carbonate solution and then hydrogenated to obtain .omega.-glucopyranpsyl-.omega.'amino-polyethyleneglycol. Aminoglyco-pyranosyl terminated polyethyleneglycol may then react with N-DPGS-succinimide to form the lipid bearing saccharide DPGS-NH-PEG-Glucose. In certain embodiments, the targeting ligands target cancer cells or tumor cells.

Detailed Description Text (356):
As one skilled in the art will recognize, any of the stabilizing materials and/or vesicle compositions may be lyophilized for storage, and reconstituted or rehydrated, for example, with an aqueous medium (such as sterile water, phosphate buffered solution, or aqueous saline solution), with the aid of vigorous agitation. Lyophilized preparations generally have the advantage of greater shelf life. To prevent agglutination or fusion of the lipids and/or vesicles as a result of lyophilization, it may be useful to include additives which prevent such fusion or agglutination from occurring. Additives which may be useful include sorbitol, mannitol, sodium chloride, glucose, dextrose, trehalose, polyvinyl-pyrrolidone and poly(ethylene glycol) (PEG), for example, PEG 400. These and other additives are described in the literature, such as in the U.S. Pharmacopeia, USP XXII, NF XVII, The United States Pharmacopeia, The National Formulary, United States Pharmacopeial Convention Inc., 12601 Twinbrook Parkway, Rockville, Md. 20852, the disclosure of which is hereby incorporated herein by reference in its entirety.

Detailed Description Text (439):
1.5 g of a fluorescein-derivatized diacylphosphatidyl ethanolamine and 3 g of soybean oil were agitated in a vortex mixer. Diacylphosphatidyl ethanolamine was derivatized with fluorescein by methods known in the art including those described by Ahlers et al, Biophys. J, 63:823-838 (1992), the disclosure of which is hereby incorporated by reference herein in its entirety. To this mixture was added 1.0 g of a lipid blend comprising 82 mol % dipalmitoylphosphatidylcholine, 10 mol % dipalmitoylphosphatidic acid and 8 mol % dipalmitoylphosphatidylethanol-amine-PEG5000 (all phospholipids from Avanti Polar Lipids, Alabaster, Ala.). The mixture was stirred for 10 minutes at 50.degree. C. then transferred into a container with 200 mls normal saline plus 1% w/v Pluronic F-65 and emulsified with a Microfluidizer (10.times.) at 16,000 psi while the temperature was maintained at 50.degree. C. The material was then subdivided into 1.0 ml aliquots in 1.5 ml vials. The vials were vacuum-evacuated, and the headspace was filled with perfluorobutane. The vials were sealed and shaken on an ESPE Capmix for 60 seconds at 4,500 rpm (alternatively, the vials may be placed on a Wig-L-Bug (Crescent Dental, Lyons Ill.) and agitated at 2800 rpm for 2 minutes). The resulting product was a suspension of a fluorescent lipid in oil filled liposomes or lipospheres (i.e., vesicles) containing about 0.45% by weight fluorophore and 0.45% by weight other lipids. The final product comprised acoustically and optically active lipospheres instilled with perfluorobutane gas, with a mean diameter under 10 .mu.m.

Other Reference Publication (125):
Calzavara-Pinton et al., "Photodynamic therapy with systemic administration of photosensitizers in dermatology", J. Photochem. Photobiol. B: Biol., 1996, 36, 225-231.

Other Reference Publication (135):
Geze et al., "Lysosomes, a key target of hydrophobic photosensitizers proposed for photochemotherapeutic applications", J. Photochem. Photobiol. B: Biol., 1993, 20, 23-35.

Other Reference Publication (138):
Jori, "Tumour photosensitizers: approaches to enhance the selectivity and efficiency of photodynamic therapy", J. Photochem. Photobiol. B: Biol., 1996, 36, 87-93.

Other Reference Publication (147):

Peng et al., "Correlation of Subcellular and Intratumoral Photosensitizer Localization with Ultrastructural Features After Photodynamic Therapy", Ultrastructural Path., 1996, 20, 109-129.

Other Reference Publication (148):
Reddi, "Role of delivery vehicles for photosensitizers in the photodynamic therapy of tumours", J. Photochem. Photobiol. B: Biol., 1997, 37, 189-195.

Other Reference Publication (153):
Spikes, "New Trends in Photobiology (Invited Review) Chlorins as Photosensitizers in Biology and Medicine", J. Photochem. Photobiol. B: Biol., 1990, 6, 259-274.

CLAIMS:

11. The method of claim 1, wherein the photoactive agent is a photosensitizer.

12. The method of claim 1, wherein the photoactive agent is at least one selected from the group consisting of fluoresceins, indocyanine green, rhodamine, triphenylamines, polymethines, cyanines, phthalocyanines, naphthocyanines, merocyanines, fullerenes, oxatellurazoles, verdins, rhodins, perphycenes, sapphyrins, rubyrins, metalloporphyrins, cholesteryl 4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene-3-dodecanoate, cholesteryl 12-(N-methyl-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-dodecanate, cholesteryl cis-parinarate, cholesteryl 3-((6-phenyl)-1,3,5-hexatrienyl)phenylproprionate, cholesteryl 1-pyrenebutyrate, cholesteryl 1-pyrenedecanoate, cholesteryl 1-pyrenehexanoate, 22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-ol, 22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-yl cis-9-octadecenoate, 1-pyrenemethyl 3-(hydroxy-22,23-bisnor-5-cholenate, 1-pyrenemethyl 3.beta.-(cis-9-octadecenoyloxy)-22,23-bisnor-5-cholenate, acridine orange 10-dodecyl bromide, acridine orange 10-nonyl bromide, 4-(N,N-dimethyl-N-tetradecylammonium)methyl-7-hydroxycoumarin) chloride, 2-dodecylresorufin, 4-heptadecyl-7-hydroxycoumarin, 5-hexadecanoyl-aminoeosin, N-octadecyl-N'-(5-(fluoresceinyl))-thiourea, octadecyl rhodamine B chloride, 2-(3-(diphenylhexatrienyl)propanoyl)-1-hexadecanoyl-sn-glycero-3-phosphoch oline, 6-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)hexanoic acid, 1-hexadecanoyl-2-(1-pyrenedecanoyl)-sn-glycero-3-phosphocholine, 1,1'-dioctadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate, 12-(9-anthroyloxy)oleic acid, 5-butyl-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene-3-nonanoic acid, N-(lissamine rhodamine B sulfonyl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt, phenylglyoxal monohydrate, naphthalene-2,3-dicarbox-aldehyde, 8-bromomethyl-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indace ne, o-phthaldialdehyde, lissamine rhodamine B sulfonyl chloride, 9-anthronitrile, 1-pyrenesulfonyl chloride, 4-(4-(dihexadecylamino)styryl)-N-methylpyridinium iodide, texaphyrins, texaphyrin-metal chelates, chlorins, chlorin e6, bonellin, mono-L-aspartyl chlorin e6, mesochlorin, mesotetraphenylisobacteriochlorin, mesotetraphenyl-bacteriochlorin, hypocrellin B, purpurins, octaethylpurpurin, zinc(II) etiopurpurin, tin(IV) etiopurpurin, tin ethyl etiopurpurin, lutetium texaphyrin, photofrin, protoporphyrin IX, tin protoporphyrin, porphyrins, benzoporphyrins, haematoporphyrin, methyl pheophorbide-.alpha.-(hexyl-ether), porphycenes, ketochlorins, sulfonated tetraphenylporphines, .delta.-aminolevulinic acid, chlorophyll, carotenoids, flavonoids, bilins, phytochromes, phycobilins, phycoerythrin, phycocyanines, retinoic acid, retinoins and retinates.

38. The method of claim 28, wherein the photoactive agent is a photosensitizer.

39. The method of claim 25, wherein the photoactive agent is at least one selected from the group consisting of fluoresceins, indocyanine green, rhodamine, triphenylamines, polymethines, cyanines, phthalocyanines, naphthocyanines, merocyanines, fullerenes, oxatellurazoles, verdins, rhodins, perphycenes, sapphyrins, rubyrins, metalloporphyrins, cholesteryl 4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene-3-dodecanoate, cholesteryl 12-(N-methyl-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-dodecanate, cholesteryl cis-parinarate, cholesteryl 3-((6-phenyl)-1,3,5-hexatrienyl)phenylproprionate,

cholesteryl 1-pyrenebutyrate, cholesteryl 1-pyrenedecanoate, cholesteryl 1-pyrenehexanoate,
22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-ol,
22-(N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-23,24-bisnor-5-cholen-3.be ta.-yl cis-9-octadecenoate, 1-pyrenemethyl 3-(hydroxy-22,23-bisnor-5-cholenate,
1-pyrenemethyl 3.beta.-(cis-9-octadecenoyloxy)-22,23-bisnor-5-cholenate, acridine orange 10-dodecyl bromide, acridine orange 10-nonyl bromide,
4-(N,N-dimethyl-N-tetradecylammonium)methyl-7-hydroxycoumarin) chloride,,
2-dodecylresorufin, 4-heptadecyl-7-hydroxycoumarin, 5-hexadecanoyl-aminoeosin,
N-octadecyl-N'-(5-(fluoresceinyl))-thiourea, octadecyl rhodamine B chloride,
2-(3-(diphenylhexatrienyl)propanoyl)-1-hexadecanoyl-sn-glycero-3-phosphoch oline,
6-N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl)amino)hexanoic acid,
1-hexadecanoyl-2-(1-pyrenedecanoyl)-sn-glycero-3-phosphocholine,
1,1'-dioctadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate,
12-(9-anthroyloxy)oleic acid,
5-butyl-4,4-difluoro-4-bora-3a,4a-diaza-s-indacene-3-nonanoic acid, N-(lissamine rhodamine B sulfonyl)-1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine, triethylammonium salt, phenylglyoxal monohydrate, naphthalene-2,3-dicarbox-aldehyde,
8-bromomethyl-4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indace ne,
o-phthaldialdehyde, lissamine rhodamine B sulfonyl chloride, 9-anthronitrile,
1-pyrenesulfonyl chloride, 4-(4-(dihexadecylamino)styryl)-N-methylpyridinium iodide,
texaphyrins, texaphyrin-metal chelates, chlorins, chlorin e6, bonellin,
mono-L-aspartyl chlorin e6, mesochlorin, mesotetraphenylisobacteriochlorin,
mesotetraphenyl-bacteriochlorin, hypocrellin B, purpurins, octaethylpurpurin,
zinc(II) etiopurpurin, tin(IV) etiopurpurin, tin ethyl etiopurpurin, lutetium texaphyrin, photofrin, protoporphyrin IX, tin protoporphyrin, porphyrins,
benzoporphyrins, haematoporphyrin, methyl pheophorbide-.alpha.-(hexyl-ether),
porphycenes, ketochlorins, sulfonated tetraphenylporphines, .delta.-aminolevulinic acid, chlorophyll, carotenoids, flavonoids, bilins, phytochromes, phycobilins,
phycoerythrin, phycocyanines, retinoic acid, retinoins and retinates.